IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application No.	:	08/716,169
Applicants	:	Stephen M. Anderton et al.
Filed	:	December 17, 1996
Title	:	**"Peptide Fragments of Microbial Stress Proteins and Pharmaceutical Composition Made Thereof for the Treatment and Prevention of Inflammatory Diseases"**
Group Art Unit	:	1644
Examiner	:	Patrick J. Nolan, Ph.D.

MAIL STOP APPEAL BRIEF - PATENTS
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

REPLY BRIEF

Sir:

This Reply Brief is submitted in reply to the Examiner's Answer dated December 19, 2003.

This Reply Brief is being submitted because the Examiner's Answer specifically asserts in a new way that Anderton et al., "Peptide-based immunotherapy of autoimmunity: a path of puzzles, paradoxes and possibilities," Immunology, 104, 367-376 (2001), is somehow inconsistent with the claimed invention and its enablement. This Reply

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450 on February 19, 2004.

Kimberly N. Welday
(Typed name of person depositing mail)

Kimberly N. Welday 02/19/2004
Signature Date

Brief explains not only why the Anderton et al. reference does not detract from patentability, but also why Wendling et al., "A Conserved Mycobacterial Heat Shock Protein...," The Journal of Immunology, 164, 2711-2717, (2000), corroborates appellant's assertions regarding enablement. Because the asserted enablement rejection is the only remaining issue in the patent application and on appeal, the Board of Patent Appeals and Interferences is requested to reverse the rejection of the Examiner and to allow pending claims 24-30.

The Board will appreciate that the Anderton et al. reference is focussed on the complexities of certain areas of APL technology. Thus, in view of its thesis, it would not be expected to highlight APLs for which no complicating aspects were known. The Anderton et al. reference does not portray heat shock proteins in any negative light, and the fact that the claimed heat shock proteins are not plagued by immunogenic unpredictability has already been documented of record.

The Examiner's Answer broadly asserts that Anderton et al. argued against the use of APLs in human autoimmune disorders, citing page 370, in the paragraph bridging columns one and two. However, the context of the cited paragraph is the difficulty of converting Th1 clones in a manner unrelated to the claimed invention, and the Examiner's Answer therefore errs in attempting to extend the cited conclusion to heat shock proteins. Heat shock peptides according to the invention act by a different mechanism, as corroborated by Wendling et al. (see below). The only mention by Anderton et al. of heat shock proteins ("hsp") is on page 368, second column, approximately in the middle of the page as follows:

> APL of MBP(72-85) and the arthritis-related peptide 180-188 of mycobacterial heat shock protein 65 (hsp 65) were generated that showed increased binding affinities for the RT1B^{l} rat class II molecule... [and] in co-immunization experiments it was found that the MBP APL specifically inhibited EAE but not arthritis, indicating direct effects on antigen-specific T cells.

Therefore, Anderton et al. refers both to MBP and to hsp APL, but then offers a conclusion only as to the MBP; the effects of the hsp 65 are not disclosed at all.

The broad conclusion cited in the Examiner's Answer is taken from page 370 of Anderton et al., which is about 1500 words after the description of hsp 65 in Anderton et al., is separated by three intervening section headings, and as mentioned above does not refer

to heat shock proteins. The reference to "antagonist or immune-deviating APL" on page 370 would not have been understood to refer to heat shock proteins because the paragraph on page 370 refers to a Th1 clone conversion mechanism that Wendling et al. had already shown the year before (see below) would not apply to heat shock proteins. Therefore, the Examiner's Answer mischaracterizes the conclusions of Anderton et al., in which there are no negative representations or implications regarding heat shock proteins. Any controversy with respect to other non-heat shock protein APLs and any inability to achieve a different mechanism is irrelevant to the claimed invention.

Parenthetically, the arthritis-related peptide 180-188 of mycobacterial heat shock protein 65, disclosed by the Anderton et al. reference, is not within the scope of the instant claims in any case.

The second of two positions set forth on page two of the Examiner's Answer relates to routes of administration. Assuming the Board considers Wendling et al. to be properly of record even though its publication date is after the present priority date, Wendling et al. actually supports the invention's having been enabled. Wendling et al. (which identifies as authors two of the present inventors) confirms that the nasal route of administration of the claimed peptides had the *in vivo* effect appellants have asserted all along. Wendling et al. states in the last sentence of the introduction that, "the data presented here suggest that the induction of IL-10 producing cells with a regulatory phenotype is a characteristic feature of immunization with hsp." Thus Wendling et al. corroborates that the Th1 clone conversion difficulties, addressed the following year by Anderton et al., do not apply to heat shock proteins, which induce IL10 producing regulatory cells.

Enablement is not precluded by the necessity for some experimentation as long as that experimentation is not undue or unduly extensive, *In re Wands*, 858 F.2d 731, 736-37 (Fed. Cir. 1988); *United States v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1988) *cert. denied*, 490 U.S. 1046 (1989). As it turns out, the inventors did identify an effective route of administration in due course. The route of administration question is characterized by Examiner Nolan as "fine tuning," and fine tuning itself implies no undue experimentation. Therefore, if the Examiner is entitled to rely on Wendling et al., then

Wendling et al. should also be credited to corroborate the very anti-inflammatory enablement which underlies the claimed invention.

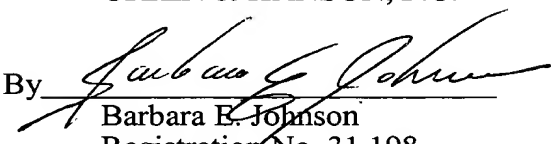
Finally, the Examiner's Answer characterizes Anderton et al. as "speaking volumes," but it is important to identify precisely about what such volumes are spoken. Anderton et al. explains that APLs may have certain effects, as described on page 367 and in Figure 1: "APL can be divided based on their ability to stimulate antigen-specific T cells." It should be appreciated that when APL is used for TCR antagonism or immune deviation, both mechanisms work only toward existing (pathogenic) Th1 T cells, namely, antagonism to silence the Th1 cells and immune deviation to induce the switch from Th1 to Th2 cells. The Examiner's Answer does not recognize that regulatory T cells, often called Tr or Treg cells, form a separate group which are completely different from Th1 and Th2. In fact, Tr cells are regulatory/inhibitory towards Th1 as well as Th2 cells. It follows that Anderton et al. does not "speak volumes" about the problems associated with APLs to induce regulatory T cells, but instead "speaks volumes" about the problems of inducing Th2 cells by switching existing Th1 cells to Th2 cells. Appellants do not agree, and Anderton et al. does not represent, that *in vivo* animal studies are problematic in predicting human treatment except as to transformation of pathogenic T cells, which Wendling et al. shows that appellants do not do. Of overriding importance is the fact that nothing within the Anderton et al. reference calls into question the assertions of the appellants with respect to the claimed heat shock peptides or their ability to function as described and claimed.

In summary, if the Board is willing to consider after-published references, appellants submit that the references should be consulted for what the references precisely say. Anderton et al. does not address the heat shock peptides set forth in the instant claims. Wendling et al. shows that the heat shock peptides of the present claims did prove to have the disclosed and claimed effect.

Reversal of the Examiner's rejections and allowance of pending claims 24-30 are respectfully requested.

Respectfully submitted,

WEBB ZIESENHEIM LOGSDON
ORKIN & HANSON, P.C.

By 

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